Cautious Optimism for Growth In Alzheimer's Disease Treatments

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Alzheimer's disease (AD), the most common form of dementia, is a progressive neurodegenerative condition that alters cognition, behavior, and functional status.[1] AD has devastating effects not only for patients but also for caregivers, who often endure physical and emotional consequences as a result of their efforts.

As of 2014, approximately 5.2 million Americans had AD, which was the sixth leading cause of death in the U.S.[2] Most AD cases occur in people older than 65 years of age.[1] As the proportion of Americans falling into this group continues to increase, the focus on AD and its treatments is also growing.

Available pharmacological options include small-molecule medications in two drug classes known as cholinesterase inhibitors and n-methyl-d-aspartate receptor antagonists. These therapies, with results that vary from person to person, are used only for symptomatic improvement—they cannot cure the disease or halt its progression.[1] Estimated U.S. sales of marketed treatments totaled $2.4 billion in 2013, a figure that is expected to more than triple to $7.6 billion in 2023 with the addition of new medications.[3]

Unmet needs in the competitive landscape of AD treatment leave significant room for future disease-modifying therapies, many of which are biologic medications.[4] Along with a promising AD pipeline, there remains an urgent need for continued research to identify curative and preventive therapies. This has become increasingly apparent as support for federal research funding grows. In addition, manufacturers, advocacy groups, and academic institutions have formed a rare partnership to evaluate upcoming AD therapies.[5,6] Such unique partnerships and increased support will facilitate the development of disease-modifying therapies for AD.

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Future Therapies

Drug *Manufacturer*	Status	Regimen Information	Pivotal Studies	Expected Approval	Anticipated Peak Year Sales/Pricing
TRx-0237 (leucomethylthioninum chloride) *TauRx Therapeutics*	Phase 3	75, 100, or 125 mg orally twice daily	NCT01689246 NCT01689233	2016	$178.8M in 2023; expected to be priced at 20–30% premium to marketed therapies but lower than mAb therapies
LuAE-58054 (idalopirdine) *Lundbeck*	Phase 3	30 or 60 mg orally once daily	STAR studies	2016	$338.5M by 2023; expected to be priced higher than medications now available
ARC-029 (nilvadipine) *Archer Pharmaceuticals*	Phase 3	8 mg orally once daily	NILVAD	2017	$1.0M in 2023; expected to be priced higher than marketed therapies but lower than mAb therapies
TTP-488 *TransTech Pharma*	Phase 3	5 mg orally once daily	NCT02080364	2017	$260.8M in 2023; expected to be priced at 30–40% premium to marketed therapies and in reference to MS, stroke, and ALS medications
EVP-6124 (encenicline) *Forum Pharmaceuticals*	Phase 3	Orally once daily; low and high dose being evaluated	NCT01969123 NCT01969136	2017	$137.1M by 2023; expected to be priced higher than medications now available
Albutein 20% + Flebogamma 5% *Grifols*	Phase 2/3	High-dose and low-dose IV infusion is being studied	AMBAR	2017	$31.4M by 2023; expected to be priced in reference to Flebogamma and Albutein

Future Therapies (continued)

Drug *Manufacturer*	Status	Regimen Information	Pivotal Studies	Expected Approval	Anticipated Peak Year Sales/Pricing
AB-1010 (masitinib) *AB Science*	Phase 3	3 or 4.5 mg/kg per day orally	NCT01872598	2017	$88.6M by 2023; expected to be priced at 30–40% premium to marketed AD treatments
MK-8931 *Merck*	Phase 3	12, 40, or 60 mg orally once daily	EPOCH: mild/moderate APECS: amnestic mild cognitive impairment	2018	$947.7M in 2023; expected to be priced at 50–60% premium to marketed medications and to use ALS medications as reference
RG-1450 (gantenerumab) *Hoffmann-La Roche*	Phase 3	SC injection every 4 weeks	Marguerite RoAD	2019	$502.2M in 2023; expected to be priced at 1–2% discount to Eli Lilly's solanezumab and in reference to IV biologic MS medications
LY-2062430 (solanezumab) *Eli Lilly*	Phase 3	400 mg IV infusion every 4 weeks	EXPEDITION	2019	$2.2 billion in 2023; as a potential first-in-class agent, not expected to be discounted
AZD-3293 *AstraZeneca*	Phase 2/3	20 or 50 mg orally once daily	AMARANTH	2019	$687.7M by 2023; expected to be priced at a 1–4% premium to Merck's MK-8931 and medications used in MS and ALS
Pioglitazone (AD-4833) *Takeda*	Phase 3	Sustained release 0.8 mg orally once daily	TOMMORROW	2020	$14.9M in 2023; expected to be priced in reference to Actos

ALS = amyotrophic lateral sclerosis; B = billions; IV = intravenous; mAb = monoclonal antibody; M = millions; MS = multiple sclerosis; SC = subcutaneous

Sources: FDA; GlobalData; manufacturers' websites; ClinicalTrials.gov

Current Therapies[a]

Drug *Manufacturer*	Approval Date	Indication[b]	Regimen Information[c]	Cost of Course of Therapy per Year[d]
Combination Cholinesterase Inhibitor and N-methyl-d-aspartate Receptor Antagonist				
Namzaric (memantine/donepezil) *Actavis*	December 23, 2014	AD	28 mg/10 mg (memantine/donepezil) orally once daily	Not available
Cholinesterase Inhibitor				
Exelon Patch (rivastigmine transdermal system) *Novartis*	July 6, 2007	AD	9.5 mg patch/24 hours	$5,487
Razadyne ER (galantamine), *Janssen*	December 22, 2004	AD	24 mg orally once daily	$4,254
Razadyne (galantamine), *Janssen*	February 28, 2001	AD	12 mg orally twice daily	$2,127
Exelon (rivastigmine) *Novartis*	April 21, 2000	AD, PD	6 mg orally twice daily	$5,021
Aricept (donepezil), *Eisai*	November 25, 1996	AD	10 mg orally once daily	$6,723
N-methyl-d-aspartate Receptor Antagonist				
Namenda XR (memantine), *Forest/Actavis*	June 21, 2010	AD	28 mg orally once daily	$4,334
Namenda (memantine), *Forest/Actavis*	October 16, 2003	AD	10 mg orally twice daily	$4,562

[a] This list is not all-inclusive; additional therapies may be available for this disease state.
[b] Abbreviated indication provided; for full indication, please refer to prescribing information.
[c] Regimens based on the recommended dosage and maintenance phases from prescribing information; typical doses and titration schedules may vary based on patient-specific requirements.
[d] Costs calculated using average wholesale price and regimen provided and rounded to the nearest dollar.

Sources: Red Book; Drugs@FDA; and prescribing information for all medications

AD = Alzheimer's disease; ER = extended release; PD = Parkinson's disease